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| 09/287,632 | 04/07/1999 | PETER MICHAEL WATERHOUSE | 021565-060 | 6526 |
| 21839 | 7590 | 03/11/2005 | EXAMINER | |
| BURNS DOANE SWECKER & MATHIS L L P | | | ZARA, JANE J | |
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| | | | 1635 | |

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/287,632

Applicant(s)

WATERHOUSE

Examiner

Jane Zara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12, 22, 26, 40, 42-44, 46, 50, 53, 54, 56, 58 and 63-108 is/are pending in the application.
- 4a) Of the above claim(s) 1-10, 12, 40, 43, 44, 46, 50, 70-84, 88-99, 104 and 105 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22, 26, 42, 53, 54, 56, 58, 63-69, 85-87, 100-103 and 106-108 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3-4-04, 6-3-04, 1-29-04, 4-5-28-04
4-7-9-03
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This Office action is in response to the communications filed 12-3-04 and 7-7-04.

Claims 1-10, 12, 22, 26, 40, 42-44, 46, 50, 53, 54, 56, 58, 63-108 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group II, claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-87, 100-103, 106-108 in the reply filed on 12-3-04 is acknowledged. The traversal is on the ground(s) that these distinct inventions have been examined previously and therefore cannot possibly constitute a serious burden on the Examiner. This is not found persuasive because the proper examination required of all of the methods claims and all of the products claims would be a serious burden to the Examiner. The methods claims include methods drawn to the use of chimeric constructs, as well as viral vectors, and include stable and transient transformation methods. The various limitations involve analyses of enablement and written description issues, and it would pose a serious burden to search the 35 methods claims drawn to utilizing these various techniques.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10, 12, 40, 43, 44, 46, 50, 70-84, 88-99, 104 and 105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12-3-04.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-87, 100-103, 106-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al in view of Brown et al and Lusky et al, the combination in view of Baracchini et al.

The claims are drawn to plant cells, plants and seeds comprising a target nucleic acid of interest and normally expressed in a plant cell, and chimeric constructs comprising a chimeric DNA comprising a promoter, operatively linked to a DNA region which, when transcribed, yields and RNA molecule capable of forming a hairpin comprising two annealing RNA sequences which comprise a sense sequence sharing

between 75 to 100% identity with between 10 and 50 consecutive nucleotides of a target nucleic acid of interest in the plant, and which further comprises a second, annealing RNA sequence comprising antisense sharing between 75 to 100% identity with between 10 and 50 consecutive nucleotides of the sense strand that targets the nucleic acid of interest, and which chimeric DNA further comprises an intron sequence heterologous to the sense strand, and optionally interposed between the sense and antisense sequences, and which chimeric DNA further comprises operably linked transcription termination and polyadenylation sequences.

Fire et al (USPN 6,506,559) plant cells, plants and their seeds comprising a nucleic acid comprising a first and second DNA sequence which expresses in the plant cell a chimeric DNA comprising a promoter, operatively linked to a DNA region which, when transcribed, yields an RNA molecule capable of forming a hairpin comprising two annealing RNA sequences which comprise a sense sequence sharing homology with consecutive nucleotides of a target nucleic acid of interest in the plant, and which further comprises a second, annealing RNA sequence comprising antisense sharing homology with the consecutive nucleotides of the sense strand that targets the nucleic acid of interest, and which chimeric DNA further comprises an intron sequence, and which chimeric DNA further comprises operably linked transcription termination and polyadenylation sequences (See the abstract, col. 3-4, col. 5, line 47-col. 6, line 54, col. 7, line 42-col. 9, line 25, col. 11, line 37-col. 12, line 8, col. 17, line 20-24, col. 21, line 36-col. 22, line 4, claims 1-4 and 7).

Fire et al do not teach the intron to be interposed between the sense and antisense strand of the chimeric construct, nor do they teach the targeting region of the chimeric construct to span between 10 and 50 consecutive nucleobases and to share between 75 to 100% identity between the sense strand and the target sequence.

Brown et al (USPN 5,859,347) teach plant cells transformed with chimeric nucleic acid expression constructs expressing desired DNA sequences, and which expression constructs comprise expression elements including operably linked promoters and further comprising heterologous introns, which introns enhance expression of the desired nucleic acid sequences in the expression construct (see col. 8, line 53-col. 9, line 17, examples 1-7 in cols. 10-18 and figures 8-27).

Lusky et al (6,350,575) teach expression constructs comprising antisense RNA and further comprising an intron as well as other expression elements including translation termination and polyadenylation signals (col. 6, line 15-col. 7, line 14).

Baracchini et al teach the ability to target a gene of interest with a complementary sequence comprising at least 10 nucleobases (see e.g. claims 1, 12, 26, and 32).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to alter the expression of a target gene of known sequence, which gene is either endogenous or heterologous to a plant cell, which target gene is either stably integrated or extrachromosomal, comprising the introduction of nucleic acids comprising sense and complementary antisense sequences of the target gene, which are operably linked to a constitutive or heterologous promoter, and which are optionally

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expressed on separate or the same expression construct, and hybridize after their expression to the complementary sequences of each other to form a double stranded molecule, whereby a duplex is formed between the expressed sense and antisense fragments, because such methods of gene silencing have been previously taught Fire et al. One of ordinary skill in the art would have expected the expressed double stranded RNA to target and inhibit the expression of corresponding target sequences of a target gene of known sequence, as taught previously by Fire et al. One of ordinary skill in the art would have been motivated to include intronic sequences within the expression constructs for gene expression in plants because the use of intronic sequences for enhancing expression of a desired gene in plants had been taught previously by Brown et al. And Lusky et al and Fire also teach the incorporation of intronic sequences in expression constructs and it was well known in the art that the inclusion of introns enhances the expression of RNA in plants. One of ordinary skill in the art would have placed the intronic sequences between the sense and antisense sequences in the chimeric construct originally taught by Fire et al because this is a design choice and additional, non-complementary sequences are included in the sense antisense constructs in order to allow for hairpin turns between complementary sequences. One of ordinary skill in the art would have expected that the intronic sequences, inserted at different places in the expression construct, would enhance expression of the chimeric constructs in plants and it would take routine experimentation to determine where in the construct the intron sequences would be inserted, as long and complementarity between the sense and antisense sequences was maintained for subsequent target

gene inhibition. One of ordinary skill in the art would have been motivated to include between 10 – 50 nucleobases for the double stranded gene silencing construct because Fire et al teaches these constructs to be in that range (e.g. 25 nucleobases) and it would take routine experimentation to vary and broaden the range of sequences of the gene silencing constructs originally taught by Fire et al. Likewise, one of ordinary skill in the art would have expected that the range of 10-50 nucleobases, and sharing between 75 to 100% homology would be effective in gene silencing, because Fire et al taught that at least 10% of the target sequences could be changed and gene silencing still occur, and successful gene targeting has been routinely provided using antisense with a minimum length of 10 nucleobases (see e.g. Baracchini et al). It would therefore take routine experimentation to alter the length of the target sequence as well as the homology required for successful gene silencing in plant cells. One would have been motivated to express downstream and operatively linked sequences in DNA expression vectors to subsequently duplex RNA in a cell to target and inhibit target gene expression. One of ordinary skill in the art would have been motivated to inhibit the expression of target genes by these expressed RNAi molecules, as described previously by Fire et al, for altering cellular phenotypes in order to study gene function, or to study the role of various target genes by comparing cellular processes in the absence or presence of these target genes expression, or to inhibit a deleterious pathogenic gene of an invading organism in a plant cell by inhibiting pathogenic target gene expression using this technique of gene silencing. One of ordinary skill in the art would have expected that the transformation of expression cassettes for target gene

silencing in appropriate plant cells, whereby the concerted expression of both the sense and antisense fragments in appropriate target cells using appropriate promoters is obtained, leads to the formation of double stranded fragments directed to the target gene sequences in the transformed cells, and consequently interferes with the expression of the target gene, thereby producing inhibition of target gene expression, allowing a comparison of cellular phenotypes in the presence and absence of target gene inhibition, as taught previously by Fire et al.

Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

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supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JZ

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